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Application No.	Ref.	Date
04 772 194.9 - 2405	M1335 EP S3	20.02.2007
Applicant: TAKARA BIO INC.		

Communication pursuant to Article 96(2) EPC

The examination of the above-identified application has revealed that it does not meet the requirements of the European Patent Convention for the reasons enclosed herewith. If the deficiencies indicated are not rectified the application may be refused pursuant to Article 97(1) EPC.

You are invited to file your observations and insofar as the deficiencies are such as to be rectifiable, to correct the indicated deficiencies within a period

of 4 months

from the notification of this communication, this period being computed in accordance with Rules 78(2) and 83(2) and (4) EPC.

One set of amendments to the description, claims and drawings is to be filed within the said period on separate sheets (Rule 36(1) EPC).

Failure to comply with this invitation in due time will result in the application being deemed to be withdrawn (Article 96(3) EPC).

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Obel, Nicolai
Primary Examiner
for the Examining Division

Enclosure(s): 4 page/s reasons (Form 2906)

Registered Letter
EPO Form 2001 07.02CSX

The examination is being carried out on the **following application documents**:

Description, Pages

1-189 as originally filed

Sequence listings, Pages

1-46 as originally filed

Claims, Numbers

1-24 as originally filed

Drawings, Sheets

1 as originally filed

1. Reference is made to the following documents; the numbering will be adhered to in the rest of the procedure:

   D1: EP 1 424 387
   D2: EP-A-1 496 109 (TAKARA BIO INC) 12 January 2005 (2005-01-12)
   D3: WO 90/13653 A (DELTA BIOTECHNOLOGY LIMITED) 15 November 1990 (1990-11-15)
   D4: EP-A-0 207 751 (DELTA BIOTECHNOLOGY LIMITED) 7 January 1987 (1987-01-07)
   D5: CELL IMMUNOL. vol. 135, no. 1, 1991, pages 105 - 117, XP002904129
   D6: US-A-5 354 686 (HABERMAN ET AL) 11 October 1994 (1994-10-11)

D7: EUR. J. IMMUNOL. vol. 21, 1991, pages 1559 - 1562, XP002961789

2. The present application does not meet the requirements of Article 52(1) EPC, because the subject-matter of claims 1-24 is not new in the sense of Article 54(2) and (3) EPC.

2.1 D1 (claim 8; paragraph 165 in combination with 77), D5 (materials and methods), D6 (Col 5 l 16-61) and D7 (abstract and p 1560 Col 1 paragraph 4) are directed to methods for the culturing of cytotoxic lymphocytes in the presence of fibronectin with either 0 or 5% plasma and the subject matter of the claims 1 and 19 is thus not novel in the sense of Art 54 EPC.

2.2 Claim 17 is directed to cytotoxic lymphocytes, however no indication exist that said lymphocytes are different from lymphocytes isolated from humans or differ from lymphocytes described in D5 (p 113 line to p 114 line 9) and D6 (Col 6 line 39 - Col 7 line 33). The applicant should please also note that the mere fact that a product is produced by an alternative method does not render the product, in this case they lymphocytes, novel (GL CIII 4.7b). The subject matter of claim 17 is therefore not novel in the sense of Art 54 EPC.

2.3 D6 (col 5 line 62-66) discloses the use of lymphocytes in therapy and said lymphocytes can also be modified for use in gene therapy (Col 37 line 41 to Col 38 line 54). The subject matter of the claims 18 and 20 is thus not new in the sense of Art 54 EPC.

2.4 The European patent application EP-A-1 496 109 (D2) published on 12.01.2005 claims the priority date of 25.03.2002.Its content as filed is therefore considered as comprised in the state of the art relevant to the question of novelty, pursuant to Article 54(3) and (4) EPC. This earlier application (claim 1) is directed to the culturing of cytotoxic lymphocytes using 5% serum and fibronectin. D2 specifies further: said lymphocytes can highly express an interleukin 2 receptor (claim 2); have a higher ratio of CD8 positive cells (claim 3); have a higher expansion fold (Table 14);

maintain high cytotoxic activity (claim 4); the fibronectin can be immobilized on solid phase (claim 5); said solid phase can be a cell culture carrier (claim 6), a petri dish, a flask or a bag (claim 7); the lymphocytes can be lymphokine-activated killer cells (example 13); the fibronectin might be any of the polypeptides with SEQ ID NO 1,2,3,5,6,7 or 8 of the present application (claim 9); the fibronectin fragment can have cell adhesion or heparin binding activity (claim 10); the fibronectin fragment can be a polypeptide selected from the group of SEQ ID NO 9-20 and 25 of the present application (claim 11); the concentration of cells in the medium at initiation of the culture should be 1 to 5.10^5 (claim 12); dilution during the culturing can be omitted (claim 13); dilution during culturing with the concentration of cells being in the range of 1.10^5 to 9.10^6 is possible (paragraph 122); the concentration of plasma can be the same after dilution of the culture as at the initiation of the culture (paragraph 130). D2 is also directed to a cytotoxic lymphocyte cultured as described in previous claims (claim 14); a medicament comprising as active ingredient a cytotoxic lymphocyte obtained by the method described in the previous claims (claim 15); a medium containing 5% serum and fibronectin (Example 3); a method comprising a step of transducing a foreign gene into a cytotoxic lymphocyte (claim 31); a method where the foreign gene is transduced using retrovirus, adenovirus adeno-associated virus or simian virus (claim 32). The invention disclosed in D2 is identical to the invention described in the claims 1-21 with the exception of the serum concentration. Claim 1 of the present application specifies that the serum concentration should be 0 or more and less than 5%, whereas D2 specifies that the serum concentration is 5%. The range of the serum concentration is not sufficiently far from the concentration known in the art as 5% will always be a more or less than 5%. It is thus not possible to distinguish the present application from the prior art. The subject matter of the claims 1-21 is thus not new in the sense of Art 54 EPC.

2.5 In D3 (plasmid pFHDEL1) and D4 (Sequence 7705) a polypeptide and nucleotide sequence with more than 98% identity to SEQ ID NO 25 and 26 are revealed and the subject matter of the claims 22-24 is thus not new in the sense of Art 54 EPC.

3. The current application should be amended as it does not conform with the rules and articles of the EPC.

3.1 Claims 2-5 do not meet the requirement of Rule 29 (3) as the claims are merely describing the effects obtained by the method of claim 1 without specifying special embodiments of the invention.

3.2 If filing amended claims care should be taken during revision, especially of the introductory portion and any statements of problem or advantage, not to add subject-matter which extends beyond the content of the application as originally filed (Article 123(2) EPC).

VOSSIUS & PARTNER

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29. Sep. 2006

EP 04 77 2194.9-2401
Takara Bio Inc.
Our Ref.: M1335 EP S3

Munich, September 28, 2006
SZ/BHU

Referring to the Communication pursuant to Art. 96(1) and Rule 51(1) EPC, we declare applicant's consent to proceed further with the application.

Dr. Friederike Stolzenburg
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